

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (twice amended) A method of screening *in vitro* for modulators of [RDGC GPCR phosphatase activity] G-protein coupled receptor signal transduction, the method comprising the steps of:

(i) providing a sample comprising a G-protein coupled receptor and a[n] recombinant RDGC phosphatase;

(ii) contacting the sample with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the sample in comparison to the level of activity in the absence of the test compound, thereby detecting a modulator of G protein coupled receptor signal transduction.

15. (twice amended) A method of screening [*in vivo*] a cell for modulators of [RDGC GPCR phosphatase activity] G-protein coupled receptor signal transduction, the method comprising the steps of:

(i) providing a cell sample comprising rhodopsin and RDGC phosphatase;

(ii) contacting the sample with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the sample in comparison to the level of activity in the absence of the test compound, thereby detecting detecting a modulator of G protein coupled receptor signal transduction..

24. (twice amended) A method of screening *in vivo* for modulators of [RDGC GPCR phosphatase activity] G-protein coupled receptor signal transduction, the method comprising the steps of:

(i) providing an animal comprising a cell comprising a G-protein coupled receptor and an RDGC phosphatase;

(ii) contacting the animal with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the animal in comparison to the level in the absence of the test compound, thereby detecting a modulator of of G protein coupled receptor signal transduction.

33. (twice amended) A method of screening *in vivo* for modulators of [RDGC GPCR phosphatase activity] G-protein coupled receptor signal transduction, the method comprising the steps of:

(i) providing an animal comprising a cell comprising rhodopsin and RDGC phosphatase;

(ii) contacting the animal with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the animal in comparison to the level in the absence of the test compound, thereby detecting a modulator of of G protein coupled receptor signal transduction.

**APPENDIX B**  
**CURRENTLY PENDING CLAIMS**

1. (twice amended) A method of screening *in vitro* for modulators of RDGC GPCR phosphatase activity, the method comprising the steps of:

(i) providing a sample comprising a G-protein coupled receptor and a recombinant RDGC phosphatase;

(ii) contacting the sample with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the sample in comparison to the level of activity in the absence of the test compound, thereby detecting RDGC GPCR phosphatase activity.

2. (cancelled) The method of claim 1, wherein the RDGC phosphatase is recombinant.

3. The method of claim 1, wherein the G-protein coupled receptor is selected from the group consisting of muscarinic receptors, neuronal nicotinic acetylcholine receptors, gamma aminobutyric acid receptors, glutamate receptors,  $\beta$ -1 adrenergic receptors,  $\beta$ -2 adrenergic receptors,  $\alpha$ -adrenergic receptors, substance K receptors, rhodopsin receptors, angiotensin receptors, dopamine receptors, nerve growth factor receptors, serotonin receptors, and taste cell receptors.

4. The method of claim 1, wherein the G-protein coupled receptor is rhodopsin.

5. The method of claim 4, wherein the rhodopsin is recombinant.

6. The method of claim 1, wherein the step of detecting comprises a G-protein coupled receptor phosphorylation assay.

7. The method of claim 1, wherein the step of detecting comprises a G-protein coupled receptor mobility assay.

8. The method of claim 1, wherein the step of detecting comprises a G-protein coupled receptor signal transduction assay.

9. The method of claim 1, wherein the sample comprises a cell.

10. The method of claim 9, wherein the cell is selected from the group consisting of a eukaryotic cell, an insect cell, a mammalian cell.

11. The method of claim 10, wherein the cell is selected from the group consisting of a *Drosophila* cell or a human cell.

12. The method of claim 1, wherein the sample comprises a membrane comprising a G-protein coupled receptor.

13. The method of claim 1, wherein the sample comprises an aqueous sample or a solid-phase sample.

14. The method of claim 1, further comprising the steps of:

(iv) providing a second sample comprising the G-protein coupled receptor and a mutant RDGC phosphatase;

(v) contacting the second sample with the test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity;

(vi) detecting RDGC GPCR phosphatase activity in the second sample;

and

(vii) comparing the level of RDGC GPCR phosphatase activity in the first sample and the second sample.

15. (twice amended) A method of screening a cell for modulators of RDGC GPCR phosphatase activity, the method comprising the steps of:

(i) providing a cell sample comprising rhodopsin and RDGC phosphatase;

(ii) contacting the sample with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the sample in comparison to the level of activity in the absence of the test compound thereby detecting RDGC GPCR phosphatase activity.

16. The method of claim 15, wherein the RDGC phosphatase is recombinant.

17. The method of claim 15, wherein the rhodopsin is recombinant.

18. (cancelled) The method of claim 15, wherein the sample comprises a cell.

19. (amended) The method of claim 18, wherein the cell is selected from the group consisting of a eukaryotic cell, a mammalian cell, an insect cell.

20. The method of claim 19, wherein the cell is selected from the group consisting of a *Drosophila* cell or a human cell.

21. (cancelled) The method of claim 15, wherein the sample comprises a membrane comprising a G-protein coupled receptor.

22. The method of claim 15, wherein the sample comprises an aqueous sample or a solid-phase sample.

23. The method of claim 15, further comprising the steps of:

(iv) providing a second sample comprising the rhodopsin and a mutant RDGC phosphatase;

(v) contacting the second sample with the test compound suspected of having the ability to modulate RDGC phosphatase activity;

(vi) detecting RDGC phosphatase activity in the second sample; and

(vii) comparing the level of RDGC phosphatase activity in the first sample and the second sample.

24. (twice amended) A method of screening *in vivo* for modulators of RDGC GPCR phosphatase activity, the method comprising the steps of:

(i) providing an animal comprising a cell comprising a G-protein coupled receptor and an RDGC phosphatase;

(ii) contacting the animal with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the animal in comparison to the level in the absence of the test compound thereby detecting RDGC GPCR phosphatase activity.

25. The method of claim 24, wherein the RDGC phosphatase is recombinant.

26. The method of claim 24, wherein the G-protein coupled receptor is selected from the group consisting of muscarinic receptors, neuronal nicotinic acetylcholine receptors, gamma aminobutyric acid receptors, glutamate receptors,  $\beta$ -1 adrenergic receptors,  $\beta$ -2 adrenergic receptors,  $\alpha$ -adrenergic receptors, substance K receptors, rhodopsin receptors, angiotensin receptors, dopamine receptors, nerve growth factor receptors, serotonin receptors, and taste cell receptors.

27. The method of claim 24, wherein the G-protein coupled receptor is rhodopsin.

28. The method of claim 27, wherein the rhodopsin is recombinant.

29. The method of claim 24, wherein the step of detecting comprises a G-protein coupled, receptor phosphorylation assay.

30. The method of claim 24, wherein the step of detecting comprises a G-protein coupled receptor mobility assay.

31. The method of claim 24, wherein the animal is selected from the group consisting of an insect and a mammal.

32. The method of claim 24, further comprising the steps of:

(iv) providing a second animal comprising a cell comprising the G-protein coupled receptor and a mutant RDGC phosphatase;

(v) contacting the second animal with the test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity;

(vi) detecting RDGC GPCR phosphatase activity in the second animal;  
and

(vii) comparing the level of RDGC GPCR phosphatase activity in the first animal and the second animal.

33. (twice amended) A method of screening *in vivo* for modulators of RDGC GPCR phosphatase activity, the method comprising the steps of:

(i) providing an animal comprising a cell comprising rhodopsin and RDGC phosphatase;

(ii) contacting the animal with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the animal in comparison to the level in the absence of the test compound thereby detecting RDGC GPCR phosphatase activity.

34. The method of claim 33, wherein the RDGC phosphatase is recombinant.

35. The method of claim 33, wherein the rhodopsin is recombinant.

36. The method of claim 33, further comprising the steps of:

- (iv) providing a second animal comprising a cell comprising the rhodopsin and a mutant RDGC phosphatase;
- (v) contacting the animal with the test compound suspected of having the ability to modulate RDGC phosphatase activity;
- (vi) detecting RDGC phosphatase activity in the second animal; and
- (vii) comparing the level of RDGC phosphatase activity in the first animal and the second animal.

37. (amended) A kit for screening for modulators of RDGC GPCR phosphatase activity, the kit comprising:

- (i) a container holding a G-protein coupled receptor and RDGC phosphatase, wherein the RDGC phosphatase has GPCR phosphatase activity; and ;
- (ii) instructions for assaying for RDGC GPCR phosphatase activity.

38. A kit of claim 37, wherein the G-protein coupled receptor and the RDGC phosphatase are recombinant.